

- 1  **Microbial Growth Control**  
Chapter 27
- 2  **27.1 Heat Sterilization**
  - Sterilization
    - kill or remove of all viable organisms within a growth medium
  - Inhibition
    - limiting microbial growth
  - Decontamination
    - treatment of an object to make it safe to handle
  - Disinfection
    - removal of all pathogens, not all microbes
- 3  **27.1 Heat Sterilization**
  - Heat sterilization
    - most widely used method
    - High temperatures denature macromolecules
    - Amount of time required to reduce viability tenfold is called the decimal reduction time
  - Some bacteria produce endospores
    - Can survive heat that would rapidly kill vegetative cells
- 4  **27.1 Heat Sterilization**
  - autoclave
    - sealed heating device that uses steam under pressure
    - Allows temperature of water to get above 100°C
    - high temperature kills not the pressure
  - Pasteurization
    - using precisely controlled heat to reduce the microbial load in heat- sensitive liquids
    - Doesn't kill all organisms so it is different than sterilization
- 5  **The Effect of Temperature Over Time on Bacterial Viability**
- 6  **The Autoclave and Moist Heat Sterilization**
- 7  **A Typical Autoclave Cycle**
- 8  **27.2 Radiation Sterilization**
  - Microwaves, UV, X-rays, gamma rays, and electrons can all reduce microbial growth
  - UV causes modifications and breaks in DNA
    - UV is useful in decontamination of surfaces
    - Cannot penetrate solid, opaque, or light-absorbing surfaces
- 9  **27.2 Radiation Sterilization**
  - Ionizing Radiation
    - produce ions and other reactive molecular species
    - Generates electrons, hydroxyl radicals, and hydride radicals
  - Some microbes more resistant to radiation than others
    - Microbes more radiation resistant than multicellular organisms
- 10  **27.2 Radiation Sterilization**
  - Radiation is used for sterilization in the medical field and food industry
  - approved by the WHO
  - decontamination of foods
    - Hamburger, chicken, spices may all be irradiated
- 11  **27.3 Filter Sterilization**
  - Filtration avoids heat for sterilization of sensitive liquids and gasses
    - Pores of filter are too small for organisms to pass through
    - Pores are large enough to allow liquid or gas to pass through

- Depth Filters
  - HEPA filters
- Membrane Filters
  - Function more like a sieve (Nucleopore filters)
- 12  **27.4 Chemical Growth Control**
  - Antimicrobial agents can be classified as
    - Bacteriostatic – inhibit growth
    - Bacteriocidal, - kill
    - Bacteriolytic - kill using cell lysis
  - Minimum inhibitory concentration (MIC)
    - smallest amount needed to inhibit growth of microbe
    - Varies with the test organism used, inoculum size, temp, pH
  - Disk diffusion assay
    - Zone of inhibition
- 13  **27.5 Chemical Antimicrobial Agents for External Use**
  - two categories
    - control in commercial and industrial applications
      - chemicals in foods, air-conditioning cooling towers, textile and paper products, fuel tanks
    - Products designed to prevent growth of human pathogens in inanimate environments and on external body surfaces
      - Sterilants kill all microbial life including endospores
      - Disinfectants kill microorganisms not necessarily endospores
      - sanitizers reduce microbial numbers
      - Antiseptics - kill or inhibit growth (nontoxic)
- 14  **Mode of Action of Some Major Antimicrobial Agents**
- 15  **Antimicrobial Spectrum of Activity**
- 16  **Annual Worldwide Production and Use of Antibiotics**
- 17  **27.6 Synthetic Antimicrobial Drugs**
  - Paul Ehrlich
    - early 1900s
    - Selective toxicity ability to inhabit or kill a pathogen without affecting the host
    - Salvarsan — one of the first effective antimicrobial drugs
  - Growth factor analogs structurally similar to growth factors but don't function in the cell
    - Analogs are known for many important biomolecules including vitamins, amino acids, and other compounds
- 18  **27.6 Synthetic Antimicrobial Drugs**
  - Sulfa drugs:
    - discovered by Gerhard Domagk in the 1930s
    - Inhibit growth of bacteria (Sulfanilamide is the simplest)
  - Isoniazid –
    - growth analog effective only against Mycobacteria
    - Interferes with synthesis of mycolic acid
  - Nucleic acid base analogs
    - formed by the addition of bromine or fluorine
  - Quinolones
    - interfere with DNA gyrase (Ciprofloxacin)
- 19  **27.7 Naturally Occurring Antimicrobial Drugs: Antibiotics**
  - Antibiotics are naturally produced antimicrobial agents

- Less than 1% of known antibiotics are clinically useful
  - modified to enhance efficacy (*semisynthetic*)
- susceptibility of microbes varies greatly
  - Gram-positive and gram-negative
    - vary in sensitivity to antibiotics such as penicillin
    - Broad-spectrum antibiotics effective against both groups
- 20  **27.8  $\beta$ -Lactam Antibiotics: Penicillins and Cephalosporins**
  - $\beta$ -Lactam
    - one of the most important groups of antibiotics
    - penicillins, cephalosporins, and cephamycins
    - Over half of all antibiotics used worldwide
  - Penicillin: discovered by Alexander Fleming
    - Primarily effective against gram-positive bacteria
    - Some synthetic forms are effective on some gram-negative
    - Target cell wall synthesis
- 21  **27.8  $\beta$ -Lactam Antibiotics: Penicillins and Cephalosporins**
  - Cephalosporins:
    - produced by fungus *Cephalosporium*
    - Same mode of action as the penicillins
    - Commonly used to treat gonorrhea
- 22  **27.9 Antibiotics from Prokaryotes**
  - Many antibiotics against *Bacteria* produced by *Bacteria*
  - Aminoglycosides
    - Ikanamycin, neomycin, amikacin, etc.
    - Not commonly used today
    - Neurotoxicity and nephrotoxicity
    - Considered reserve antibiotics for when other antibiotics fail
- 23  **27.9 Antibiotics from Prokaryotes**
  - Macrolides
    - erythromycin
    - Broad-spectrum antibiotic targets the 50S subunit of ribosome
  - Tetracyclines
    - widespread use in humans and animals
    - Broad-spectrum inhibition of protein synthesis
    - Inhibit 30S ribosome subunit functioning
- 24  **27.9 Antibiotics from Prokaryotes**
  - Daptomycin
    - Also produced by *Streptomyces*
    - Used to treat gram-positive bacterial infections
    - Forms pores in cytoplasmic membrane causing depolarization
  - Platensimycin
    - New structural class of antibiotic
    - Broad-spectrum, effective against MRSA and Vancomycin resistant enterococci
- 25  **27.10 Antiviral Drugs**
  - Most antiviral drugs also target host structures
    - resulting in toxicity
    - A few antivirals specifically target viruses
  - Most successful and commonly used
    - nucleoside analogs (AZT)
      - Block reverse transcriptase and production of viral DNA

- Also called *nucleoside reverse transcriptase inhibitors*
  - *Nonnucleoside reverse transcriptase inhibitors (NNRTI)*
    - bind directly to RT and inhibit reverse transcription
- 26  **27.10 Antiviral Drugs**
- *Protease inhibitors*
    - Inhibit processing of large viral proteins
  - *Fusion inhibitors*
    - prevent viruses from fusing with the host cell
  - Two categories of drugs successfully limit influenza infection
    - Adamantanes
    - Neuraminidase inhibitors
  - *Interferons*
    - small proteins stimulate antiviral proteins in uninfected cells
- 27  **27.11 Antifungal Drugs**
- Fungi pose special problems for chemotherapy because they are eukaryotic
    - Much of the cellular machinery is the same as that of animals and humans
    - As a result many antifungals are topical
    - There are a few drugs that target unique metabolic processes
- 28  **27.11 Antifungal Drugs**
- *Ergosterol inhibitors*
    - target fungal plasma membrane component ergosterol
  - *Echinocandins*
    - Inhibit 1,3  $\beta$ -D glucan synthase
    - Used to treat *Candida* infections
  - Other drugs target
    - chitin biosynthesis, folate biosynthesis, or disrupt microtubule aggregation
  - Antifungal-resistant fungi are emerging
- 29  **27.12 Antimicrobial Drug Resistance**
- *Antimicrobial drug resistance*
    - acquired ability to resist the effects of chemotherapeutic
  - Some ways microbes naturally resist antibiotics
    - lack structure the antibiotic inhibits
    - impermeable to antibiotic
    - inactivate the antibiotic
    - modify the target of the antibiotic
    - develop a resistant biochemical pathway
    - pump out the antibiotic (efflux)
- 30  **27.12 Antimicrobial Drug Resistance**
- drug-resistance genes located on R plasmids
  - R plasmids predate the antibiotic era
  - use of antibiotics in medicine, veterinary, and agriculture
    - select for the spread of R plasmids
    - overuse of antibiotics
    - antibiotics used in agriculture as supplements to animal feed
- 31
- 32  **27.12 Antimicrobial Drug Resistance**
- few pathogens have developed resistance to all known antimicrobial agents
    - Methicillin-resistant *S. Aureus* (MRSA)
  - Resistance minimized by using antibiotics correctly
  - Resistance can be lost if antibiotic not used for several years

33 34 **27.13 The Search for New Antimicrobial Drugs**

- Long-term solution
  - new antimicrobial compounds
  - Modification of current compounds
- Automated chemistry methods has sped up drug discovery
  - 7,000,000 compounds must be screened to find a single useful clinical drug

35 **27.13 The Search for New Antimicrobial Drugs**

- Computers used to design molecules
  - Most successful example is *saquinavir*
    - Binds to active site of HIV protease
- New methods of screening natural products
  - discovery of platensimycin
- Combinations of drugs can be used
  - ampicillin and sulbactam
- *Bacteriophage therapy*